II. Non-Technical Abstract

There are presently more than 40,000 new cases of melanoma in the U.S. per year with 7,300 melanoma-related deaths. Patients with stage III disease have at least a 50% chance of recurrence after surgical resection; patients with stage IV melanoma have a median survival of less than I year and most of these patients eventually die of melanoma. Standard therapy is dacarbazine chemotherapy, and while response rates range from 8-25%, there is little evidence that treatment improves survival. Combination chemotherapy and biochemotherapy regimens have been reported to induce higher response rates with the disadvantage of greater toxicity and, to date, there is no evidence that they result in improved survival. New approaches to the treatment of this disease are needed.

The overall goal of this study is to develop ways to treat advanced melanoma. In particular we seek to use naturally occurring melanoma tumors into which a potent immune stimulating substance will be introduced to try and create conditions for an immune response to the melanoma. The immune stimulation will be produced by the naturally occurring protein, interleukin 12. The gene for interleukin 12 will be injected directly into the tumor. Following this injection, a low electric voltage will be applied to the tumor using a specially designed apparatus. This equipment has been used previously in human beings and is known to be safe. The combination of the direct gene injection and the specially timed electric shock cause tumor cells to take up the gene and make the protein to a much larger extent than they would otherwise. This procedure will be done up to 5 times in each patient (depending on the number of tumors each patient has). Based on our animal experiments we anticipate that the tumors will regress and also that some immunity may be generated against spread of melanoma.